AMENDMENT

In the claims

Please amend the claims as follows:

1. (currently amended) A method for ~~reducing inducement of histopathological change in a target muscle tissue site resulting from application of an electric field to a subject to deliver~~ delivering a therapeutic agent ~~thereto~~ to a subject, ~~said method~~ comprising:

introducing an effective amount of at least one therapeutic agent into ~~the~~ a target muscle tissue site of a subject, wherein the therapeutic agent comprises a polynucleotide that encodes a therapeutic protein or peptide; and

generating an electric field at the target muscle tissue site ~~of the subject~~ by introducing from 1 to about 4 monopolar DC pulses, each pulse having a duration of about 10 ms to about 100 ms, to generate a nominal field strength of about 100V/cm to about 300V/cm at the target muscle tissue site~~,~~.

~~thereby reducing the inducement of histopathological change in the target muscle tissue site resulting from application of the electric field as compared to alternative methods for applying an electric field to the target muscle tissue site.~~

2. (currently amended) A ~~The~~ method ~~of~~ according to claim 1~~, wherein the~~ that reduces histopathological change at the target muscle tissue site as a result of the application of the electric field~~is associated with the induction or amplification of an immune response~~.

3. (currently amended) A ~~The~~ method ~~of~~ according to claim ~~1~~ 3, wherein the histopathological change is selected from the group consisting of inflammation, induction or amplification of an immune response, necrosis, and fibrosis.

4. (canceled)

5. (canceled)

6. (currently amended) A ~~The~~ method ~~of~~ according to claim 1, wherein the duration of each pulse is in the range from about 20 ms to about 60 ms.

7. (currently amended) A ~~The~~ method ~~of~~ according to claim 1, wherein there are no more than two pulses at each target muscle tissue site.

8. (currently amended) A ~~The~~ method ~~of~~ according to claim 1, wherein the nominal field strength is in the range from about 100V/cm to about 232V/cm.

9. (currently amended) A ~~The~~ method ~~of~~ according to claim 8, wherein the nominal field strength is in the range from about 100V/cm to about 150V/cm.

10. (currently amended) A ~~The~~ method ~~of~~ according to claim 8, wherein the duration of each pulse is in the range from about 40 ms to about 60 ms.

11. (currently amended) A ~~The~~ method ~~of~~ according to claim 1, wherein the electric field is generated by applying ~~to the subject~~ electroporation electrodes to the subject, wherein a portion of the electrodes that contacts the subject is made of a non-toxic, biocompatible metal.

12. (currently amended) A ~~The~~ method ~~of~~ according to claim 11, wherein the metal is gold.

13. (currently amended) A ~~The~~ method ~~of~~ according to claim 1, wherein the subject is a mammal.

14. (currently amended) A ~~The~~ method ~~of~~ according to claim 1, wherein the subject is a human.

15. (currently amended) An *in vivo* method for ~~enhancing expression of~~ expressing a therapeutic polypeptide or peptide encoded by an isolated polynucleotide ~~to be~~ delivered into cells in a subject, ~~said method~~ comprising:

a) introducing ~~an effective amount of~~ at least one isolated polynucleotide encoding a therapeutic polypeptide or peptide into a target muscle tissue site of a subject; and

b) generating an electric field at the target muscle tissue site by introducing from 1 to about 4 monopolar DC pulses, each having a pulse duration of about 10 to about 100 ms, to generate a nominal field strength of about 100V/cm to about 300V/cm at the target muscle tissue site~~, at substantially the same time as the introduction of the polynucleotide so as to result in the polynucleotide entering cells of the target muscle tissue for expression of the therapeutic polypeptide therein;~~

~~thereby enhancing the expression of the therapeutic polypeptide as compared to expression of the therapeutic polypeptide achieved by other methods for generating an electric field in the target muscle tissue.~~

16. (currently amended) A ~~The~~ method ~~of~~ according to claim 15~~, wherein the~~ that reduces histopathological change at the target muscle tissue site as a result of the application of the electric field~~is associated with the induction or amplification of an immune response~~.

17. (currently amended) A ~~The~~ method ~~of~~ according to claim 16, wherein the histopathological change is selected from the group consisting of inflammation, induction or amplification of an immune response, necrosis, and fibrosis.

18. (currently amended) A ~~The~~ method ~~of~~ according to claim 15, wherein the duration is in the range selected from the group consisting of from about 20 ms to about 60 ms and from about 40 ms to about 60 ms.

19. (currently amended) A ~~The~~ method ~~of~~ according to claim 15, wherein there are no more than two pulses.

20. (currently amended) A ~~The~~ method ~~of~~ according to claim 15, wherein the nominal field strength is in the range from about 100V to about 150V.

21. (currently amended) A ~~The~~ method ~~of~~ according to claim ~~33~~ 15, wherein ~~the duration of the pulses is in the range from about 40 ms to about 60 ms~~ the polynucleotide is introduced at substantially the same time as generating the electric field.

22. (currently amended) A ~~The~~ method ~~of~~ according to claim ~~33~~ 15, wherein the electric field is generated by applying to the subject electroporation electrodes, wherein a portion of the electrodes that contacts the subject is made of a non-toxic, biocompatible metal.

23. (currently amended) A ~~The~~ method ~~of~~ according to claim ~~36~~ 22, wherein the metal is gold.

24. (currently amended) A ~~The~~ method ~~of~~ according to claim ~~35~~ 15, wherein the subject is a mammal.

25. (currently amended) A ~~The~~ method ~~of~~ according to claim 15, wherein the subject is a human.

26. (currently amended) A ~~The~~ method ~~of~~ according to claim 15, wherein the polynucleotide is injected intramuscularly at from 1 to about 20 sites in the target muscle tissue.

27. (currently amended) A ~~The~~ method ~~of~~ according to claim 15, wherein said polynucleotide is selected from the group consisting of double stranded DNA, single-stranded

DNA, complexed DNA, formulated DNA, encapsulated DNA, naked RNA, encapsulated RNA, and combinations thereof.

28. (currently amended) A ~~The~~ method ~~of~~ according to claim 15, wherein the polynucleotide encoding the therapeutic polynucleotide is contained in a DNA vector.

29. (currently amended) A ~~The~~ method ~~of~~ according to claim 15, said polynucleotide being operably associated with a regulatory sequence for expression of the therapeutic polypeptide or peptide in said cells.

30. (currently amended) A ~~The~~ method ~~of~~ according to claim 15, wherein said polynucleotide further encodes a selectable marker polypeptide.

31. (currently amended) A ~~The~~ method ~~of~~ according to claim 29, wherein said regulatory sequence comprises a promoter.

32. (currently amended) A ~~The~~ method ~~of~~ according to claim 31, wherein said promoter is muscle specific.

33. (currently amended) A ~~The~~ method ~~of~~ according to claim 32, wherein said promoter is selected from CMV, RSV LTR, MPSV LTR, and SV40 promoters.

34. (currently amended) A ~~The~~ method ~~of~~ according to claim 15, wherein the electric pulses are administered to the target muscle tissue using an electroporation electrode comprising a plurality of electrically conducting needles.

35. (currently amended) A ~~The~~ method ~~of~~ according to claim 34, wherein a portion of the needles that contacts the subject is made of a non-toxic, biocompatible metal.

36. (currently amended) A ~~The~~ method ~~of~~ according to claim 35, wherein the metal is gold.

37. (currently amended) A method for delivering a polynucleotide encoding a peptide or polypeptide to a target muscle tissue site, comprising:

a) introducing an effective amount of at least one isolated polynucleotide encoding a peptide or polypeptide into a target muscle tissue site of a subject;

b) introducing at least a conductive portion of an electrode needle array into the target muscle tissue; and

c) applying from 1 to about 4 monopolar DC pulses having a duration of about 10 ms to about 100 ms each to generate a nominal field strength of about 100V/cm to about 300V/cm at the target muscle site, thereby delivering the polynucleotide to the target muscle.

38. (currently amended) A ~~The~~ method ~~of~~ according to claim 37, wherein the electrode needle array comprises four electrode needles and two pulses are applied to the target muscle tissue site to generate a nominal field strength of about 116 V/cm.